

# Ambient Temperature and External Causes of Death in Japan from 1979 to 2015: A Time-Stratified Case-Crossover Analysis

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**BACKGROUND:** Although substantial evidence suggests that high and low temperatures are adversely associated with nonaccidental mortality, few studies have focused on exploring the risks of temperature on external causes of death.

**OBJECTIVES:** We investigated the short-term associations between temperature and external causes of death and four specific categories (suicide, transport, falls, and drowning) in 47 prefectures of Japan from 1979 to 2015.

**METHODS:** We conducted a two-stage meta-regression analysis. First, we performed time-stratified case-crossover analyses with a distributed lag nonlinear model to examine the association between temperature and mortality due to external causes for each prefecture. We then used a multivariate meta-regression model to combine the association estimates across all prefectures in Japan. In addition, we performed stratified analyses for the associations by sex and age.

**RESULTS:** A total of 2,416,707 external causes of death were included in the study. We found a J-shaped exposure–response curve for all external causes of death, in which the risks increased for mild cold temperatures [20th percentile; relative risk (RR) = 1.09 (95% confidence interval [CI]: 1.05, 1.12)] and extreme heat [99th percentile; RR = 1.24 (95% CI: 1.20, 1.29)] compared with those for minimum mortality temperature (MMT). However, the shapes of the exposure–response curves varied according to four subcategories. The risks of suicide and transport monotonically increased as temperature increased, with RRs of 1.35 (95% CI: 1.26, 1.45) and 1.60 (95% CI: 1.35, 1.90), respectively, for heat, whereas J- and U-shaped curves were observed for falls and drowning, with RRs of 1.14 (95% CI: 1.03, 1.26) and 1.95 (95% CI: 1.70, 2.23) for heat and 1.13 (95% CI: 1.02, 1.26) and 2.33 (95% CI: 1.89, 2.88) for cold, respectively, compared with those for cause-specific MMTs. The sex- and age-specific associations varied considerably depending on the specific causes.

**DISCUSSION:** Both low and high temperatures may be important drivers of increased risk of external causes of death. We suggest that preventive measures against external causes of death should be considered in adaptation policies. <https://doi.org/10.1289/EHP9943>

## Introduction

External causes of death are death caused by acute exposure to physical agents such as mechanical energy, heat, electricity, chemicals, and ionizing radiation and the broad categories include transport, falls, drowning, suicide, homicide, and other external causes.<sup>1</sup> According to the Global Health Estimates 2016 reported by the World Health Organization (WHO), the transport, falls, and suicide categories were the 4th, 17th, and 18th leading causes of death, respectively, in the WHO Western Pacific Region.<sup>2</sup> The number of external causes of death steadily increased between 1990 and 2016, and the identification of potential risk factors for external causes of death and cause-specific categories is required.<sup>3,4</sup>

Extreme weather events are a significant public health concern. Although substantial evidence has suggested the risks of cold and heat on mortality, as reviewed by Song et al.,<sup>5</sup> a small number of previous studies have examined the relationship between temperature and cause-specific mortality, including external causes.<sup>6,7,8,9</sup> These studies have reported that heat or heat waves were associated with

an increased risk of external causes of death.<sup>6,7,8,9</sup> A study from Estonia showed that both extreme cold and heat increased all external causes of death.<sup>10</sup> A recent study in the United States reported that a 1.5°C anomalously warm year would lead to an additional 1,601 [95% confidence interval (CI): 1,430; 1,776] injury deaths.<sup>11</sup>

Given that each specific category of external causes of death has unique characteristics, which death rates varied by season, sex, and age<sup>12</sup> and investigating the extent to which temperature is adversely associated with each specific cause and subgroups by sex and age is warranted. Furthermore, Mitchell et al.<sup>13</sup> indicated that some potential flaws in previous studies (e.g., a small sample size, use of monthly averaged temperature and health data, and a linear assumption for the association) may limit the validity of their findings.<sup>6,8,10,11,14</sup> More rational assumptions and approaches are needed to provide more accurate estimates, particularly for the short-term associations between temperature and cause-specific external causes of death, which would ultimately help decision makers formulate prevention measures and policies targeted at specific causes.

In the present study, we examined the short-term associations between temperature and external causes of death and four most common specific categories (i.e., suicide, transport, falls, and drowning) in Japan from 1979 to 2015, taking into account the nonlinear and delayed influence of the temperature–mortality association. We hypothesized that the nonlinear shapes of the exposure–response curves might differ according to the specific categories of external causes of death. We also examined whether the associations differed by sex and age.

## Methods

### Data Collection

We collected death certificate data for external causes of death and daily weather variables from 47 prefectures in Japan from 1 January 1979 to 31 December 2015. The daily counts of external

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causes of death, including stratification by sex and age groups, were transformed from a computerized death certificate database maintained by the Ministry of Health, Labor and Welfare of Japan. Informed consent was not needed given that we obtained deidentified data. All external causes of death were categorized according to the 9th and 10th revisions of the *International Statistical Classification of Diseases and Related Health Problems* (ICD-9<sup>15</sup>; ICD-10<sup>16</sup>): ICD-9 codes E800–E999 and ICD-10 codes V01–Y98. Cause-specific external causes of death outcomes included suicide (ICD-9 codes E950–E958; ICD-10 codes X60–X84), transport (ICD-9 codes E800–E848; ICD-10 codes V01–V99), falls (ICD-9 codes E880–E888; ICD-10 codes W00–W19), and drowning (ICD-9 codes E910; ICD-10 codes W65–W74).

Meteorological data were obtained from hourly measurements provided by the Japan Meteorological Agency for a single weather station in the capital city of each prefecture (except for two prefectures with a station adjacent to the capital city), including data on mean ambient temperature (in degrees Celsius), relative humidity (in percentage), and daily total precipitation (in millimeters). We calculated the daily mean dew point temperature as a measure of humidity using mean temperature and relative humidity.<sup>17,18</sup> The daily amount of precipitation was categorized into three levels: a) sunny days with no precipitation, b) lower than the 50th percentile, and c) over the 50th percentile for each prefecture.

### Statistical Methods

A two-stage meta-analysis was conducted using multi-prefectural daily time-series data. In the first stage, a time-stratified case-crossover design for each prefecture was used to estimate the association between mean temperature and each health outcome. In the second stage, a multivariate meta-regression analysis was used to combine prefecture-specific estimates across all 47 prefectures. All statistical analyses were performed using R software (version 3.5.2; R Development Core Team).

**First-stage modeling.** We used a time-stratified case-crossover design with a distributed lag nonlinear model (DLNM) based on a conditional quasi-Poisson regression model for each prefecture.<sup>19,20</sup> We incorporated a time stratum in the model to adjust for seasonality and long-term time trends, which is equivalent to the case-control days matching in the time-stratified case-crossover design by the same day-of-week within the same month in the same year.<sup>19</sup> To explore the associations of mean temperature on all and four categories of external causes of death, we used a quadratic B-spline for the exposure–response association, with two internal knots equally located at the 33rd and 66th percentiles of prefecture-specific temperature distributions. This choice for the optimal number of knots was based on minimizing the quasi-Akaike information criteria.<sup>21</sup> We also applied the maximum lag of up to 14 d using a natural cubic spline with three equally spaced knots on a log scale to examine the delayed influence of the nonlinear exposure–response associations. The maximum lag days were guided by country-level lag–response associations for external causes of death in our initial analyses (Figure S1), which showed that the cold risks on all external causes of death and drowning lasted for 14 d. Furthermore, the 3-d moving average dew point temperature (a natural cubic spline with three degrees of freedom), precipitation (categorical variable), and public holidays (binary variable) were included in the model as time-varying confounders. Strata with no death counts were excluded from the analysis (Table S1).

Based on the lag-cumulative nonlinear temperature–mortality associations fitted in the model above, we quantified heat and cold risks on the all and four categories of external causes of death, expressed as the relative risk (RR) for heat and cold temperatures compared with the risk for minimum mortality temperature (MMT), where the minimum risk was identified between the 1st and 99th

percentiles of temperature. Given that the exposure–response curves varied considerably in four categories, different MMTs were chosen for each health outcome and each prefecture accordingly. Different temperature percentiles for cold and heat were also chosen for each health outcome, where the highest risks were identified below or above the MMTs, given the restriction of the range between the 1st and 99th percentiles of temperature.

**Second-stage modeling.** To combine the prefecture-specific results estimated from the first-stage modeling, we performed a multivariate meta-regression based on a random-effect model.<sup>22</sup> To better explain the between-location variability, we included the prefecture-specific mean temperature and temperature range in the model as meta-predictors. To investigate heterogeneity, we calculated the  $I^2$  and tested the multivariate extension of the Cochran's  $Q$  statistic.<sup>23,24</sup> In addition, from the model fit, the best linear unbiased prediction was used to predict prefecture-specific estimates. When calculating the prefecture-specific RRs, we used the fixed percentiles of temperature for cold or heat across prefectures (which were the same as those at the country level), although the MMTs varied among the prefectures. Furthermore, we used a univariate meta-regression with the prefecture-specific log(RR) and the corresponding standard errors by adding several prefecture-level variables (longitude, latitude, average of mean temperature, range of mean temperature, average of dew point temperature, and median of daily total precipitation) one at a time and then estimated the ratio of RR, indicating how the prefecture-specific RRs changed per unit increase in each prefecture-level variable.

### Subgroup Analysis

We performed stratified analyses by sex (males and females) and two age groups (<65 y for younger people and ≥65 y for older people) using the same first- and second-stage modeling above. When pooling the cumulative RRs in each subgroup, we used the same temperature percentiles for MMT, cold, and heat used in the total population.

### Sensitivity Analysis

To assess the robustness of our results, we performed several sensitivity analyses. First, we changed the number of knots from two knots at the 33rd and 66th percentiles to three knots at the 25th, 50th, and 75th percentiles for the mean temperature. Second, we changed the maximum lag period from 14 to 7 d. Third, we changed the cutoff to define the categorized precipitation from the relative measure of the 50th percentiles for each prefecture to the same absolute measure at the median of prefecture-level average precipitation across all 47 prefectures (i.e., 6.6 mm). Lastly, we repeated the analyses with the exclusion of outliers for the daily external causes of death that occurred as a result of the great earthquake disasters in Japan. We defined potential outliers as five times the interquartile range over the 75th percentile for each prefecture on the earthquake dates (Table S2).

### Results

A total of 2,416,707 external causes of death were included in this study, accounting for 6.89% of all causes of mortality during the same period in Japan (Table 1). Of the total number of cases, more than half of the deaths were males for all external causes (65.53%) and its cause-specific (suicide: 68.08%, transport: 71.90%, falls: 61.23%, and drowning: 57.80%). For all external causes (55.84%), suicide (73.42%), and transport (66.39%), the majority of cases occurred in younger people, whereas older people accounted for the majority of death counts for falls (70.85%) and drowning (65.54%). Table 2 shows the distributions of prefecture-level

**Table 1.** Descriptive statistics for external causes of death from 1979 to 2015 in Japan.

Categories	External causes	Suicide	Transport	Falls	Drowning
Total number of deaths	2,416,707	933,126	438,465	211,278	184,525
Male (%)	1,583,666 (65.53)	635,273 (68.08)	315,235 (71.90)	129,357 (61.23)	106,652 (57.80)
Female (%)	833,041 (34.47)	297,853 (31.92)	123,230 (28.10)	81,921 (38.77)	77,873 (42.20)
Younger (%) <sup>a</sup>	1,349,501 (55.84)	685,114 (73.42)	291,111 (66.39)	61,594 (29.15)	63,557 (34.40)
Older (%) <sup>a</sup>	1,066,845 (44.14)	247,842 (26.56)	147,342 (33.60)	149,680 (70.85)	120,942 (65.54)
Female to male death ratio <sup>b</sup>	0.53	0.47	0.39	0.63	0.73
Older to younger death ratio <sup>c</sup>	0.79	0.36	0.51	2.43	1.90
Daily mean (SD)	178.80 (163.77)	69.05 (17.55)	32.45 (12.29)	15.63 (5.65)	13.65 (8.46)

Note: SD, standard deviation.

<sup>a</sup>There were 361 (0.015%), 170 (0.018%), 12 (0.003%), 4 (0.002%), and 26 (0.014%) deaths missing age information on all external, suicide, transport, falls, and drowning, respectively.

<sup>b</sup>The total death number ratio between female and male from 1979 to 2015.

<sup>c</sup>The total death number ratio between older and younger people (younger, <65 years of age; older, ≥65 years of age) from 1979 to 2015.

average weather variables, ranging from 9.0°C to 23.1°C for daily mean temperature, 3.5°C to 18.0°C for daily dew point temperature, and 3.6 mm to 12.1 mm for daily total precipitation. Tables S3 and S4 show the summary statistics of external causes of death and weather variables for each prefecture.

Figure 1 shows the pooled exposure–response curve of the overall lag-cumulative association between mean temperature and all external causes of death and the spatial distribution of RRs for cold and heat in 47 prefectures in Japan. The association between temperature and all external causes of death was nonlinear, and MMT was identified at the 72nd percentile of temperature. The highest risk for cold was reached at the 20th percentile of temperature for all external causes of death with an RR of 1.09 [95% CI: 1.05, 1.12], and a significant heat risk was observed with an RR of 1.24 (95% CI: 1.20, 1.29) at the 99th percentile compared with those for the MMT (Table 3). The RRs for cold tended to be higher in the southern prefectures, whereas those for heat were higher in the northern prefectures (Figure 1B,C). The country-level lag–response curves for all external causes of death show the delayed effects for cold and heat lasted for 14 d and 5 d, respectively (Figure S1).

Figure 2 shows the exposure–response curves for each cause-specific external cause of death. The shapes of the curves varied depending on the causes, in which the risks of suicide and transport monotonically increased as temperature increased, whereas the estimated curves for falls and drowning were J- and U-shaped, respectively. Given the different exposure–response curves among health outcomes, different MMTs and the percentiles of temperature for cold and heat were chosen to calculate the RR (Table 3 and Figure 2). For suicide and transport, only heat risks were observed with RRs of 1.35 (95% CI: 1.26, 1.45) and 1.60 (95% CI: 1.35, 1.90), respectively, compared with those at the first percentile of temperature. For falls, the RRs for cold and heat were estimated to be 1.13 (95% CI: 1.02, 1.26) and 1.14 (95% CI: 1.03, 1.26), respectively, compared with those for the MMT at the 19th percentile of temperature. The RRs of drowning were larger than those for other specific causes and were estimated to be 2.33 (95% CI: 1.89, 2.88) for cold and 1.95 (95% CI: 1.70, 2.23) for heat compared with those at the 77th percentile of temperature. The lag–response patterns for cause-specific

categories varied considerably (Figure S1). In general, the risks of drowning for cold or heat lasted longer than those for suicide, transport, and falls.

Figure 3 shows the spatial distribution of RRs in the 47 prefectures for cause-specific external causes of death. In general, the RRs of suicide, falls, and drowning for heat were higher in the northern prefectures (Figure 3A,D,F, respectively), whereas the RRs of drowning for cold were higher in the southern prefectures (Figure 3E). The prefecture-specific RRs are listed in Table S5A,B.

In the meta-regression analysis, the residual heterogeneity was reduced slightly when the prefecture-level mean temperatures and temperature ranges were included as predictors (Table S6). The multivariate Cochran's *Q* test for heterogeneity was significant for all external causes, transport, and drowning ( $p < 0.001$ ). Furthermore, the Wald test results showed that the prefecture-level mean temperature or temperature range could explain, in part, the heterogeneity across prefectures for all external causes, suicide, and drowning ( $p < 0.05$ ). Table S7 and Figure S2 show how the prefecture-specific RRs changed by each prefecture-level variable. Specifically, the RRs of all external causes and drowning for cold were positively associated with higher levels of mean temperature (warmer prefectures) and dew point temperature (more humid prefectures), whereas they were negatively associated with temperature range, longitude, and latitude, suggesting larger RRs for cold were observed in southern (or western) prefectures. In contrast, the RRs for heat were negatively associated with mean temperature and dew point temperature in general, suggesting that RRs for heat were larger in colder and less humid prefectures. Larger RRs for heat were also associated with temperature range, longitude, and latitude, reflecting northern (or eastern) prefectures. The RRs of transport for heat were positively associated with higher levels of precipitation.

Figure 4 depicts the pooled cumulative RRs in the stratified analysis by sex and age groups. We observed that the RRs of all external causes, suicide, falls, and drowning differed among the subgroups, and CIs were generally not overlapping. Specifically, the RRs of all external causes of death for both cold and heat were higher in females and older people than in males and younger people (Figure 4A,B). Similar patterns were observed in the RRs of suicide for heat (Figure 4C). We also found higher RRs of falls for cold in older people and heat in males (Figure 4E,F). For drowning, the RRs for cold were higher in females and older people (Figure 4G), whereas the opposite pattern was observed for heat, with higher RRs in males and younger people (Figure 4H). Corresponding numeric data are shown in Table S8.

Sensitivity analyses showed that the association estimates were generally robust given the altered conditions for the knots of temperature, lag days, and precipitation, except for falls (Table S9). When we applied a shorter maximum lag of up to 7 d, the highest risk of falls for heat shifted from the 88th to 99th percentile of

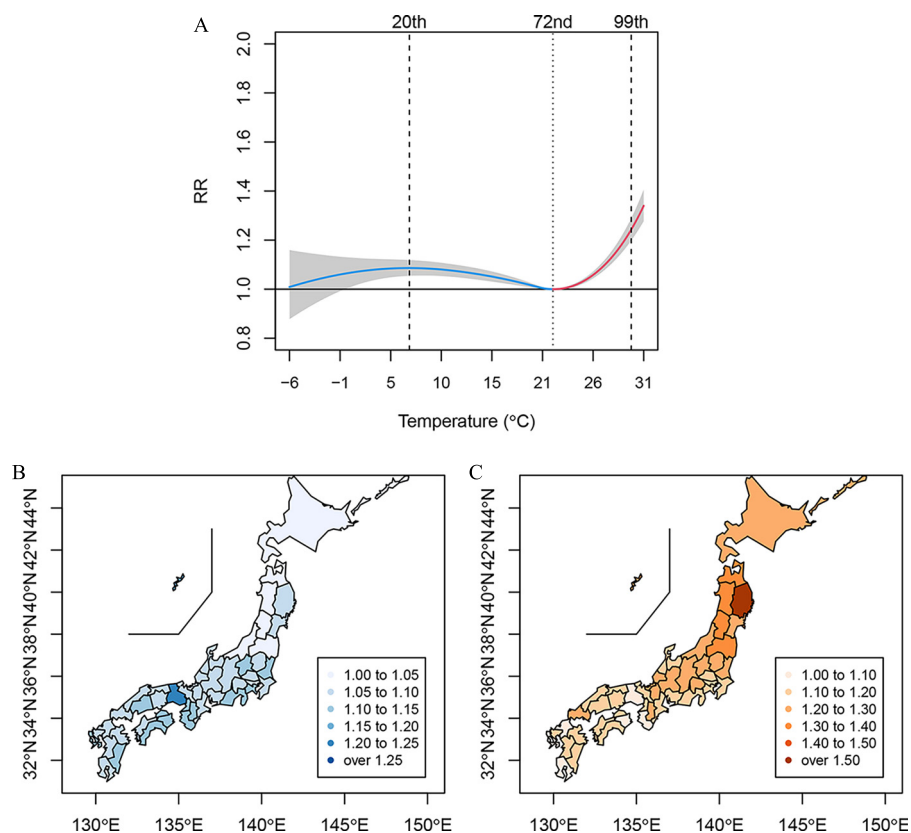
**Table 2.** Summary statistics for weather variables from 1979 to 2015 in country level.

Weather variables	Mean	SD	Minimum	25th	Median	75th	Maximum
Mean temperature (°C) <sup>a</sup>	15.2	2.3	9.0	14.4	15.9	16.5	23.1
Dew point temperature (°C) <sup>a</sup>	9.5	2.2	3.5	8.5	9.9	10.3	18.0
Daily precipitation (mm) <sup>a</sup>	6.6	1.9	3.6	5.5	6.6	7.8	12.1

Note: SD, standard deviation; 25th and 75th are percentiles.

<sup>a</sup>The summary statistics were calculated based on the prefecture-level averages of each weather variable.





**Figure 1.** Exposure–response curve and spatial map of prefecture-specific relative risks (RRs) for all external causes of death. (A): Exposure–response curve with 95% CIs (shaded region) for all external causes of death, estimated by using a conditional Poisson model adjusting for seasonality, long-term time trend, day of week, holiday, dew point temperature, and precipitation. Vertical lines indicate the locations for minimum mortality temperature (MMT) and RRs calculation of cold (below the MMT) and heat (above the MMT) risks, respectively. (B) and (C): Spatial map of prefecture-specific RRs of cold and heat. MMTs varied by prefecture, and the locations for RRs calculation were the 20th and 99th percentiles of each prefecture mean temperature. See Table 3 for the corresponding numeric data. Note: CI, confidence interval.

temperature, and the RR of falls for cold became nonsignificant (Figure S3). In addition, the association estimates and exposure–response curves changed only slightly after excluding data outliers due to great earthquake disasters (Table S9 and Figure S4).

## Discussion

In the present study, we investigated the short-term association between ambient mean temperature and external causes of death

in Japan using a two-stage design. The exposure–response curves between temperature and external causes of death were nonlinear and differed for specific causes. We found that both cold and heat exposures were associated with an increased RR of all external causes of death, falls, and drowning, whereas only heat risks were observed for suicide and transport.

Our results showed that both moderately low and extremely high temperatures were associated with a high risk of all external causes of death. These results are partly consistent with those of previous studies that reported the risks of ambient temperature on death due to external causes.<sup>6,7,8,9,10,11,25</sup> Orru and Åström<sup>10</sup> found significantly high RRs of mortality due to external causes for heat and cold (with lag04) using a time-series analysis in Estonia. A recent study observed that a 1.5°C anomalously warm year would be associated with a total of 1,601 (95% CI: 1,430; 1,776) additional injury deaths using a Bayesian spatiotemporal model in the United States.<sup>11</sup> Other studies have focused only on exploring the risks of heat or heatwave,<sup>6,7,8,9</sup> and all reported significantly increased RRs of high temperatures on external causes of death.

For each cause-specific category, we found heat risks only on suicide and transport, whereas we found J- and U- shaped exposure–response curves for falls and drowning. Previous studies have demonstrated that high temperatures increased the risk of suicide and transport,<sup>26,27,28,29,30</sup> which is consistent with our findings. However, studies focusing on the associations between temperature and fatal falls and drowning are limited. Some studies found that reduced temperatures increased the incidence of wrist or hip fractures in older people,<sup>31,32</sup> as well as the presence of higher wrist fracture risk with increased temperature in

**Table 3.** Pooled RRs of all and cause-specific external causes of death in Japan.

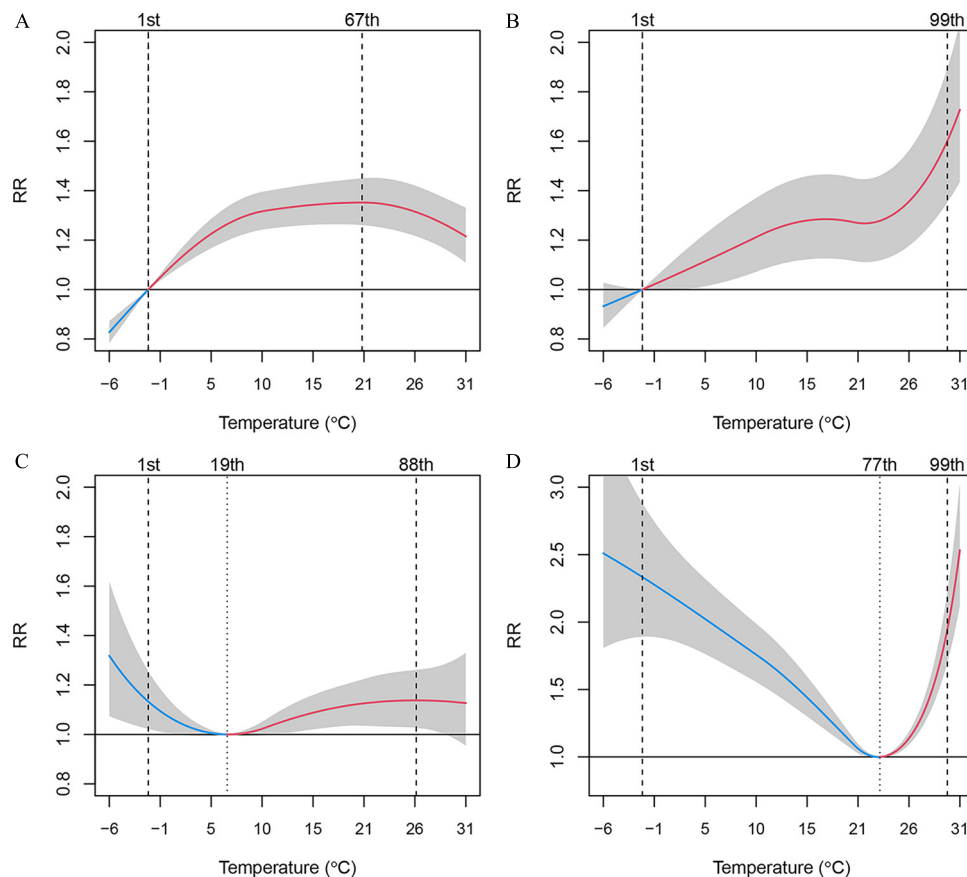
Outcomes	Temperature percentile <sup>a</sup>			RRs (95% CI) compared with MMT	
	Cold <sup>b</sup>	MMT <sup>c</sup>	Heat <sup>b</sup>	Cold risk	Heat risk
External causes	20	72	99	1.09 (1.05, 1.12)	1.24 (1.20, 1.29)
Suicide	NA	1	67	NA	1.35 (1.26, 1.45)
Transport	NA	1	99	NA	1.60 (1.35, 1.90)
Falls	1	19	88	1.13 (1.02, 1.26)	1.14 (1.03, 1.26)
Drowning	1	77	99	2.33 (1.89, 2.88)	1.95 (1.70, 2.23)

Note: Pooled cumulative RRs with 95% CIs for all and cause-specific external causes of death, estimated by using a conditional Poisson model adjusting for seasonality, long-term time trend, day of week, holiday, dew point temperature, and precipitation. CI, confidence interval; MMT, minimum mortality temperature (percentile); NA, Not Applicable; RR, relative risk.

<sup>a</sup>The percentiles of the temperature for centering and RR calculation.

<sup>b</sup>The percentiles of the temperature for estimating cold (heat) risks, where the highest risks were identified below or above the MMTs, given the restriction of the range between the 1st and 99th percentiles of temperature.

<sup>c</sup>The percentile of minimum mortality temperature, where the minimum risk was identified between the 1st and 99th percentiles of temperature in country level.



**Figure 2.** Exposure-response curves with 95% CIs (shaded region) for cause-specific external causes of death, estimated by using a conditional Poisson model adjusting for seasonality, long-term time trend, the day of week, holiday, dew point temperature, and precipitation. (A) suicide; (B) transport; (C) falls; and (D) drowning. Vertical lines indicate the location for minimum mortality temperatures (MMTs) and relative risks (RRs) calculation for cold (below the MMTs) or heat (above the MMTs) risks. See Table 3 for the corresponding numeric data. Note: CI, confidence interval.

younger men, which could be related to fatal falls. Other studies have reported that warmer temperatures increase the risk of fatal drowning or drowning hospitalization.<sup>33,34,35</sup> Parks et al.<sup>11</sup> explored the risks of temperature on falls and drowning together and showed cold or heat risks on falls among different age groups and only heat risk on drowning.

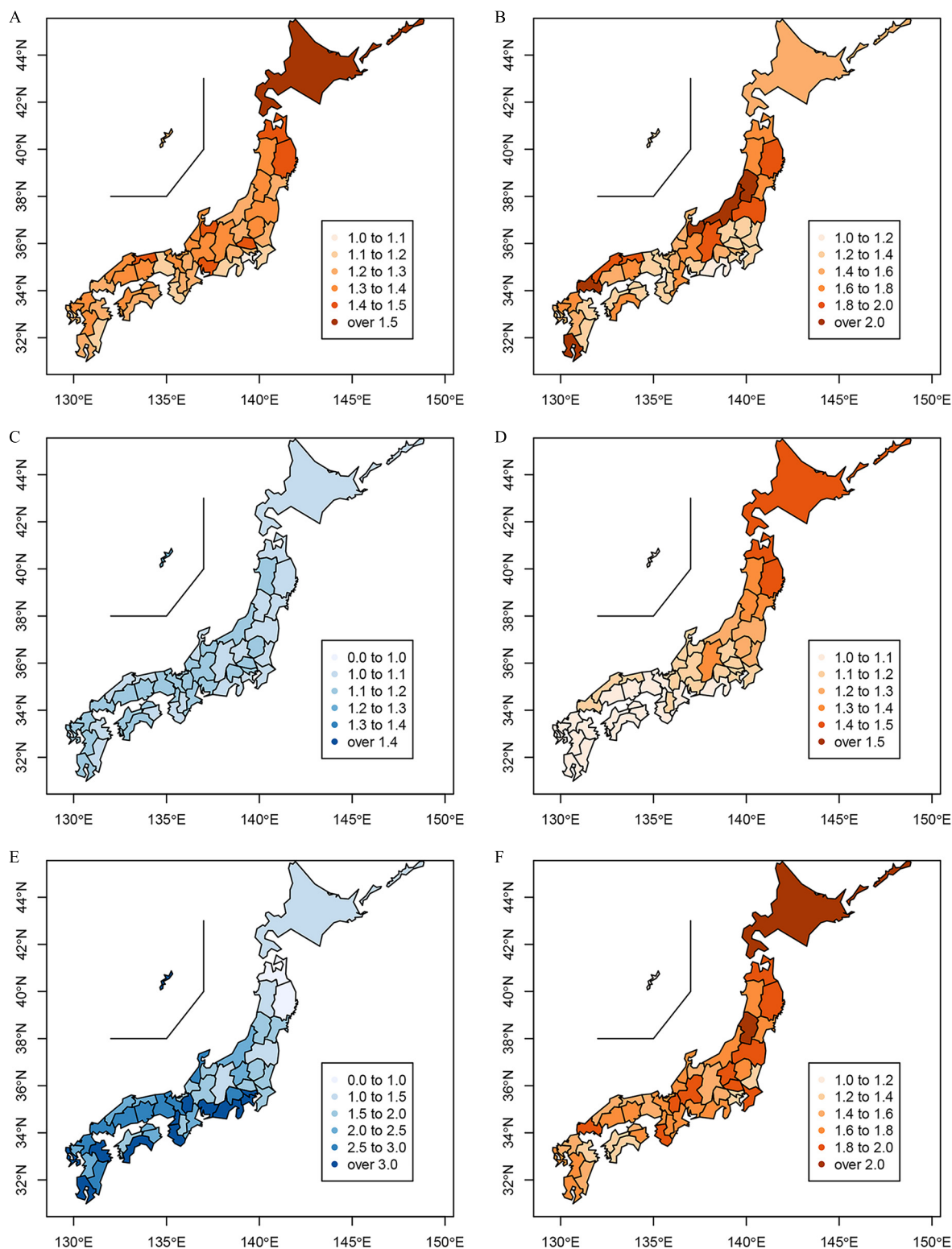
A notable finding of our cause-specific analyses was that the high RR of drowning for cold (RR = 2.33; 95% CI: 1.89, 2.88) was mostly attributed to older people (Figure 4G). Hsieh et al.<sup>36</sup> reported that the unintentional drowning mortality rates for older people in Japan were highest among 31 Organization for Economic Co-operation and Development (OECD) countries, and over 70% of deaths involved bathtubs in 2014. We speculated the high RR of drowning for cold can be explained by Japan's unique bathing manner,<sup>36,37,38</sup> characterized by head-out water immersion and high frequency of bathing. One potential explanation could be that older people generally have a weaker thermoregulatory system than younger people and that some underlying diseases or etiologies (e.g., acute ischemic heart failure, heat-stroke, and blood pressure fluctuation) triggered during bathing in winter could induce a higher risk of drowning.<sup>39,40,41,42</sup>

To date, the biological mechanisms underlying the association between ambient temperature and external causes of death are unclear. Some plausible behavioral and physiological pathways have been suggested to explain these associations, which also help to interpret why the RRs differed greatly by sex and age groups. Suicide studies have hypothesized that variations in serotonin levels with temperature may lead to suicide.<sup>43,44</sup> Regarding transport, driving performance deteriorates at warm temperatures,<sup>45,46</sup> which

could potentially increase the rate of traffic accidents. People, especially young men, are more likely to engage in sports and outdoor activities during warmer conditions,<sup>31,47</sup> which partly explains the higher RR of falls for heat in males and younger people than in females and older people. The higher RR of falls for cold in older people than in younger people could be due to slippery conditions with ice or snow in winter.<sup>48,49</sup> Swimming is likely to be more common when the temperature is higher, leading to a higher risk of drowning accidents; this behavior also differs by sex and age.<sup>50</sup> The cold risks on drowning in this study may be related to Japanese bathing culture.<sup>36</sup>

The abovementioned explanations might underlie the different lag-response patterns between external causes of death and non-accidental mortality, and the latter one has been commonly observed up to 21 d for cold risks.<sup>22</sup> In the present study, we observed the cold risks on all external causes and drowning lasted for 14 d, the lag-response patterns for heat risks varied by specific causes. We presumed that the shorter lag-response associations for external causes of death could be greatly influenced by human behaviors compared with nonaccidental mortality, which cardiorespiratory diseases largely account for. Further studies are warranted to validate the different lag patterns.

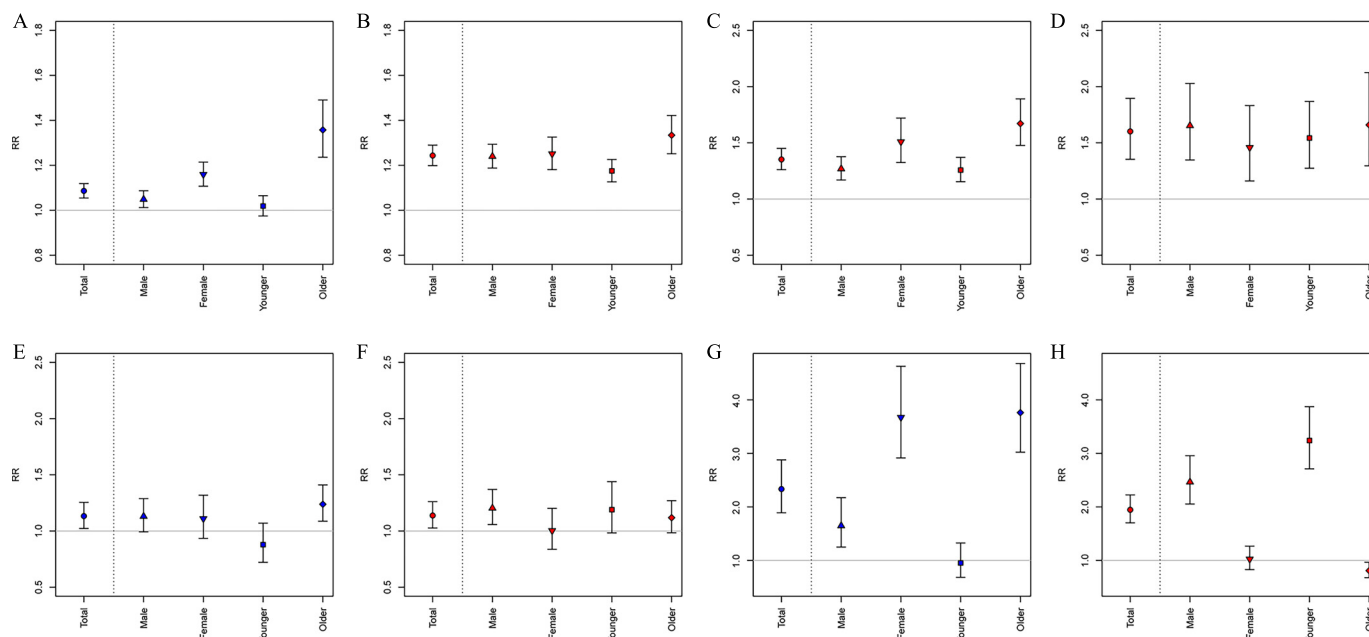
This study has several strengths. First, we estimated the short-term associations between temperature and all and cause-specific external causes of death using a time-stratified case-crossover design with DLNM. This modeling framework can depict the non-linear and delayed association between temperature and external causes of death, allowing us to examine the exposure-response curves more precisely. In addition, applying the unified analytical



**Figure 3.** Spatial map of prefecture-specific relative risks (RRs) for cause-specific external causes of death. (A) RR of suicide for heat; (B) RR of transport for heat; (C) RR of falls for cold; (D) RR of falls for heat; (E) RR of drowning for cold; and (F) RR of drowning for heat. The prefecture-specific RRs were calculated using the same percentiles of temperature across prefectures for heat (i.e., the 67th for suicide, 99th for transport, 88th for falls and 99th for drowning) and for cold (i.e., the 1st for both falls and drowning), compared with those at the prefecture-specific minimum mortality temperatures (MMTs). See Tables S5A,B for the corresponding numeric data.

method makes the exposure–response curves and estimates comparable for each health outcome. Second, we investigated the associations at both the national and prefectural levels using long-term time-series data over 30 y and a relatively large sample size, which

was a result of the higher suicide and drowning rates in Japan than in other countries in the OECD.<sup>51,52</sup> Finally, the heterogeneous climate conditions from north to south in Japan also helps to investigate the spatial variation of the risks for cold and heat.



**Figure 4.** Pooled cumulative relative risks (RRs) with 95% CIs (vertical bars) for external causes of death in subgroup analyses by sex and age groups (younger, <65 years of age; older, ≥65 years of age), estimated by using a conditional Poisson model adjusting for seasonality, long-term time trend, the day of week, holiday, dew point temperature, and precipitation. (A) RR of external causes for cold; (B) RR of external causes for heat; (C) RR of suicide for heat; (D) RR of transport for heat; (E) RR of falls for cold; (F) RR of falls for heat; (G) RR of drowning for cold; and (H) RR of drowning for heat. See Table S8 for the corresponding numeric data. Note: CI, confidence interval.

However, several limitations of this study need to be addressed. First, we used the ambient mean temperature at the prefecture level as exposure, because only prefecture-level aggregated data of mortality were available. This exposure measurement error, known as Berkson error, may reduce the precision or power of effects (wider CI).<sup>53,54</sup> Second, although we considered potential confounders by the study design in our model, some time-varying covariates were not included in this study, such as air pollution, air conditioner use, and time spent outdoors. Third, the high RR of drowning for cold might not be generalized to other regions or countries given that we hypothesize that this finding may be driven by the unique bathing culture in Japan. Further studies are needed to provide evidence and confirm our results.

The present study highlights that a nonlinear relationship exists between ambient temperature and external cause of death; this relationship could be further stratified by sex and age. Given that extreme warm and cold events will continue to increase in the future,<sup>55</sup> proactive public health adaptation strategies for climate change for all and vulnerable target populations would be necessary. Public health interventions to encourage a change in people's behaviors by taking temperature into account may be particularly useful because external causes of death could be greatly influenced by human behaviors.

## Conclusion

Our findings indicated the presence of a nonlinear relationship between ambient mean temperature and external causes of death in Japan. Both cold and heat were associated with increased risk of mortality due to external causes; the shapes of the exposure-response curves varied according to the specific causes, including suicide, transport, falls, and drowning. The associations differed by sex and age groups, which also varied depending on the specific causes. This study provides evidence that preventive measures targeted for total and vulnerable populations against external causes of death, in conjunction with nonaccidental mortality, should be considered in future adaptation policies.

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